Atty's Docket: 101195-67

REMARKS

Claims 1-6 and 9-10 are pending in the application.

Examiner's objections and rejections are addressed below.

All claims have been amended and new claims 11-13 have been added. No amendment introduces new matter.

Specification

The abstract has been replaced with a new replacement abstract of less than 150 words.

§ 112, 2nd paragraph

Claims 2, 3, 5, 6, 9 and 10 have been amended to address Examiner's comments.

It is believed that these rejections should be withdrawn.

§ 102

Applicants' method is directed to process which would be useful for identifying patients that are likely to benefit from a specific regimen of treatment with one or more compounds and/or radiation therapy. None of the cited references teach or suggest this method.

Further, as described in detail below, none of the cited references indicate that mutations that disrupt certain genes, e.g., p53, may be indicators of a patient's selective resistance to one or more particular therapeutic agents.

Last, Examiner is respectfully reminded that in her restriction requirement, she asserted that protein analyses and nucleic analyses comprise patentably distinct methods. However, in all the cited references, the analyses are either protein gels or light microscopy of cells. For example, in Harris, Figures 1-5 are protein gels that do not even relate gene expression profiling.

Fig. 6 in Harris shows the effect of a peptide complex on a generic *in vitro* transcription system. This also has nothing to do with the claimed method as it is merely an experiment describing the peptide complex's effect transcription.

Thus, Examiner cannot properly employ Harris as providing an anticipatory and/or enabling disclosure in relation to the claimed method.

Similar arguments are provided below in relation to the additional references.

For this reason, all prior rejections should be withdrawn.

§ 102a and § 102e – anticipation by Harris.

Harris teaches methods of using compounds causing that induce apoptosis. Harris's focus is on site-specific mutagenesis studies on p53, and the effect of the mutation on inducing apoptosis. From these studies, Harris designs compounds which, we note are preferred peptides corresponding to regions of the p53 protein. See col. 11. There is no operative or enabled teaching of any treatment based on any compound's effect on p53 expression or any other gene.

Nor is their any evidence that these peptide compounds are chemotherapeutic as is required in the claimed method.

The claimed method does not induce or examine apoptosis. The claimed method employs the *ex vivo* treatment of cells/tissues from human patients and correlates its pattern of gene expression to a patient's responsiveness, or lack thereof, to compounds and/or radiation.

It is respectfully requested that this rejection be withdrawn.

2. § 102e by Fung

The foregoing remarks provided to overcome the Harris reference are equally appropriate with respect to the Fung reference. Fung does not show the effect of a single compound on the expression profile of any gene in explanted tissue from human patients.

Instead, Fung uses only transfected cells expressing exogenous genes. This cannot anticipate and/or enable the instantly claimed method. The cellular material used in the claimed method is freshly prepared from patients. Further, these cells are not transfected and therefore are not expressing foreign genes.

Also a key distinction is that Fung does not teach the use of gene expression profiles in any manner whatsoever. Fig. 14, cited by Examiner are simply light micrographs of transfected cells. As indicated by Examiner's restriction requirement and the foregoing comments, tthis analysis has nothing to do with the claimed method.

In accordance, it is respectfully requested that the rejection based on the Fung reference be withdrawn.

§ 103(a) – Obviousness over Stoughton, in view of Harris

Stoughton shows a sophisticated generic method for dealing with data. Specifically, Stoughton method addresses the effects of multiple drugs on gene expression levels. However, Examiner is incorrect in concluding that because Stoughton's technique may teach how investigators may analyze certain results, Stoughton does not provide *any* enabling disclosure or suggestion or examples that correspond to the claimed method.

In addition, there would be absolutely no motivation or suggestion to combine Stoughton's method with Harris's teachings because Harris could not even use Stoughton's method of data handling. This is because Harris does not teach or suggests even a single experimental protocol and/or piece of data that is addressed by

Stoughton. In other words, Stoughton's method does not address issues in the art raised by the work of Harris and/or Fung.

In sum, persons of ordinary skill in the art would not combine the teachings of Harris (and/or Fung) with Stoughton. The combined references do not suggest *ex vivo* treatments of human tissues with the recited compounds and/or radiation. Nor do they suggest any relevant correlations between the expression of the p53 and/orother genes with the patient's tissues' responsiveness or resistance to these compounds.

Respectfully, the rejection over Stoughton and Harris should be withdrawn.

Respectfully, the rejection of claim 9 over Spengler is should be withdrawn, as it does not teach each limitation of claim 9.

CONCLUSION

Favorable and early action is respectfully requested.

It is believed that all objections and rejections have been addressed. Applicants are hopeful that the very substantial differences between the claimed method and the references have been clearly elucidated.

It is respectfully requested that all rejections be withdrawn and all claims be allowed.